

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/14078

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A01K67/033 C07K14/435 C12Q1/68

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01K C07K C12Q

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	BOEHNI R ET AL: "AUTONOMOUS CONTROL OF CELL AND ORGAN SIZE BY CHICO, A DROSOPHILA HOMOLOG OF VERTEBRATE IRS1-4" CELL, CELL PRESS, CAMBRIDGE, MA, US, vol. 97, no. 7, 25 June 1999 (1999-06-25), pages 865-875, XP000877263 ISSN: 0092-8674 page 870, column 2, paragraph 2 "Experimental Procedures" page 872, column 2, paragraph 3 -page 873, column 2, paragraph 1 --- -/--	52-54

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

* Special categories of cited documents:

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

4 May 2004

Date of mailing of the international search report

13/05/2004

Name and mailing address of the ISA

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>LEEVERS S J ET AL: "THE DROSOPHILA PHOSPHOINOSITIDE 3-KINASE DP110 PROMOTES CELL GROWTH" EMBO JOURNAL, OXFORD UNIVERSITY PRESS, SURREY, GB, vol. 15, no. 23, 1996, pages 6584-6594, XP000877417 ISSN: 0261-4189 cited in the application the whole document</p>	52-54
A	<p>RORTH P ET AL: "SYSTEMATIC GAIN-OF-FUNCTION GENETICS IN DROSOPHILA" DEVELOPMENT, COMPANY OF BIOLOGISTS, CAMBRIDGE,, GB, vol. 125, no. 6, March 1998 (1998-03), pages 1049-1057, XP000863084 ISSN: 0950-1991 cited in the application "Material and Methods" "Discussion" abstract</p>	52-54
A	<p>NAGASE T ET AL: "PREDICTION OF THE CODING SEQUENCES OF UNIDENTIFIED HUMAN GENES VII. THE COMPLETE SEQUENCES OF 100 NEW CDNA CLONES FROM BRAIN WHICH CAN CODE FOR LARGE PROTEINS IN VITRO" DNA RESEARCH, UNIVERSAL ACADEMY PRESS, JP, vol. 4, no. 2, 1997, pages 141-150, XP001052821 ISSN: 1340-2838 cited in the application the whole document</p>	1-18, 24-51
A	<p>WO 00/78940 A (HAFEN ERNST ;UNIV ZUERICH (CH)) 28 December 2000 (2000-12-28) the whole document</p>	52-54
A	<p>DJORDJEVIC S ET AL: "Structural insight into substrate specificity and regulatory mechanisms of phosphoinositide 3-kinases" TIBS TRENDS IN BIOCHEMICAL SCIENCES, ELSEVIER PUBLICATION, CAMBRIDGE, EN, vol. 27, no. 8, 1 August 2002 (2002-08-01), pages 426-432, XP004373664 ISSN: 0968-0004 the whole document</p>	52-54

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	<p>KOZMA SARA C ET AL: "Regulation of cell size in growth, development and human disease: PI3K, PKB and S6K." BIOESSAYS: NEWS AND REVIEWS IN MOLECULAR, CELLULAR AND DEVELOPMENTAL BIOLOGY. ENGLAND JAN 2002, vol. 24, no. 1, January 2002 (2002-01), pages 65-71, XP009030256 ISSN: 0265-9247 the whole document</p>	52-54

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Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:

Although claims 1-18 and 40-49 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☒ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:

see FURTHER INFORMATION sheet PCT/ISA/210
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.2

Claims Nos.: 1-18 (partially), 19-23 (completely), 24-51 (partially) and 55-57 (completely)

The subject-matter of independent claim 1 and of dependent claims 2-9 is fundamentally unclear (Article 6 PCT) for the following reasons:

The expression "pathological conditions associated with dysregulation of the insulin pathway" has no well-recognised meaning in the art and leaves the skilled reader in doubt with regard to its scope. The only definition provided by the description (page 16, lines 1-3) is that this expression "includes, but is not limited to", diabetes and Type A syndrome of insulin resistance.

In view of the numerous biochemical pathways wherein the insulin pathway might be involved (see for instances all the documents mentioned in the search report), a meaningful search could only be carried out for diabetes and Type A syndrome of insulin resistance.

The expression "a modulator of a protein" also has no well-recognised meaning in the art. Moreover, this expression only describes a desirable property of the entity but does not define said entity in terms of technical features. The use of this expression hence leaves the skilled reader in doubt with regard to its exact scope. This lack of clarity is further increased by the reference to "a protein selected from the group consisting of those disclosed in Table 4 or Table 5" (see below). In the present case, a meaningful search could only be carried out for the modulator classes mentioned in the description, i.e. those explicitly mentioned in e.g. dependent claims 5 (see also below) and 8.

In view of the content of Tables 4 and/or 5, the expression "a protein selected from the group consisting of those disclosed in Table 4 or Table 5" is absolutely unclear. This lack of clarity arises from the fact that the tables do not disclose/describe proteins. In fact, these tables appear to relate to Drosophila genes, some of them being referred to as "unknown", to transcripts and to "best human homologues".

In view of the description, it appears that said expression "a protein selected from the group consisting of those disclosed in Table 4 or Table 5" should be understood as referring to the proteins coded by the best human homologues (see e.g. page 2, lines 12-15). It is however to be noted that for a number of the Drosophila genes listed in the tables no human homolog is indicated. Moreover, others have merely been "predicted by automated computational analysis" and/or their function is not known, so that it is absolutely not possible to search for a modulator of their function.

In Example 1, three Drosophila genes and their best human homologues (PDK, SHP-2 and KIAA0336) have been identified, using the method of independent claim 52, as being "genetic modifiers" of the insulin pathway. Of these three genes, only EP(3)3459/KIAA0336 is disclosed (twice in Table 4: page 57, line 19 and page 59, line 13) in Table 4 or 5 and is therefore claimed.

The fundamental lack of clarity of independent claim 1 and of dependent

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

claims 2-9 makes it impossible to perform a meaningful search of the subject-matter of these claims over their whole scope. With regard to the subject-matter of claims 1-9, the International Search has therefore been limited to:

A method to treat, prevent or ameliorate diabetes or Type A syndrome of insulin resistance comprising administering to a subject a effective amount of a modulator as defined in claims 5 of 8 of the protein coded by the KIAA0336 gene.

The subject-matter of claims 10-18 does not differ from that defined in claims 1-9. The search of subject-matter of these claims has hence also been restricted accordingly.

The subject-matter of claims 19-23 relies on the biochemical function of the protein disclosed in Table 4 or 5, i.e. protein coded by the KIAA0336 gene (see above). Since the protein coded by the KIAA0336 gene does not have a known function (see the description: page 54, lines 12-13), a meaningful search of the subject-matter of these claims is not possible.

Moreover, the arguments presented with regard to the subject-matter of claims 1-9 also apply for the subject-matter of claims 24-51, the search of which also been restricted accordingly.

In addition, the subject-matter of independent claim 55 and dependent claims 56 and 57 refer to genetic modifiers identified according to the method of claim 52.

Such a genetic modifier is however not a product produced by the screening method of claim 52, which relate to methods of identification. It is rather a product that has been identified using said method. The mere fact that the genetic modifier has been identified by the method of screening method of claim 52 is however not a technical feature of said modifier. Moreover, this fact does not provide any information regarding possible technical features of said modifier.

Since the modifiers of claims 55-57 are not defined in terms of technical features, it is not possible to perform a meaningful search of their subject-matter.

The applicant's attention is drawn to the fact that claims, or parts of claims, relating to inventions in respect of which no international search report has been established need not be the subject of an international preliminary examination (Rule 66.1(e) PCT). The applicant is advised that the EPO policy when acting as an International Preliminary Examining Authority is normally not to carry out a preliminary examination on matter which has not been searched. This is the case irrespective of whether or not the claims are amended following receipt of the search report or during any Chapter II procedure.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 03/14078

Patent document cited in search report	Publication date	Patent family member(s)	Publication date	
WO 0078940	A	28-12-2000	WO 0078940 A1	28-12-2000
			AU 4160599 A	09-01-2001
			CA 2375484 A1	28-12-2000
			EP 1187912 A1	20-03-2002
			JP 2003503677 T	28-01-2003